

II. **AMENDMENTS TO THE SPECIFICATION**

*{Please amend the paragraph at page 1, lines 5-11, as indicated below:}*

B<sup>1</sup> The present invention relates to a test to be used to screen large populations for the occurrence of cancer. The method is based on the measurement of tissue inhibitor of metalloproteinases 1 (TIMP-1) in body fluids. The invention permits the early identification of patients having colorectal cancer. The method is highly specific, and patients with non-malignant conditions, such as inflammatory ~~bowl~~ bowel diseases, are not detected. Measurement of another similar inhibitor, TIMP-2, does not demonstrate equivalent clinical value, indicating an additional level of specificity of the invention.

*Please amend the paragraph starting at page 4, line 31 as indicated below:*

B<sup>2</sup> Specificity is defined as the proportion of non-diseased individuals ~~positives (i.e. individuals having a parameter representing the concentration of TIMP-1 in body fluid samples higher than a predefined diagnostic level)~~ that are correctly identified by the described method of the invention. Sensitivity is defined as the proportion of diseased individuals ~~negatives (i.e. individuals having a parameter representing the concentration of TIMP-1 in body fluid samples lower than a predefined diagnostic level)~~ that are correctly identified by the described method.

*Please amend page 7, lines 25-34, as indicated below:*

B<sup>3</sup> In Example 5 it is shown that total TIMP-1 levels are significantly higher in patients with colorectal cancer than in patients with inflammatory ~~bowl~~ bowel diseases (IBD), showing that total TIMP-1 can be used to screen for colorectal cancer in a population of patients with IBD. That TIMP-1 is not increased in non-malignant diseases

B<sup>3</sup>  
is supported by a recent paper, (Keyser *et al*, 1999), demonstrating that patients with rheumatoid arthritis do not have increased plasma TIMP-1 levels. Also, by comparing total TIMP-1 levels among patients with IBD (excluding patients with clinically assessed acute active disease, n=4) and healthy blood donors, no significant differences in total plasma TIMP-1 levels were found (p=0.56), showing that these non-malignant diseases do not give false positive test results.

---

*Please amend page 37, lines 1-4, as indicated below:*

**Abstract**

~~The present invention describes a method for determining whether an individual is suffering from cancer by determining a parameter representing the TIMP-1 concentration in body fluid samples from the individual.~~

*Please add new page 47, after page 46 and before Fig. 1, attached herewith as Tab 1, which contains the ABSTRACT.*

**ABSTRACT**

B4 The present invention describes a method for determining whether an individual is likely to have cancer by determining a parameter representing the TIMP-1 concentration in body fluid samples from the individual.